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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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13. ABSTRACT *(Maximum 200 words)*

Work by Prof. Fujimoto and his collaborators is summarized here

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DEPARTMENT OF ELECTRICAL ENGINEERING AND COMPUTER SCIENCE

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September 28, 1994

Captain Pat Roach
Armstrong Laboratory
AL/OEOP
Brooks Air Force Base
Texas 78235

Dear Pat:

Enclosed please find the technical report and completed AFOSR questionare for our subcontract F49620-93-1-0301 entitled "Mechanisms and Diagnostics of Ultrashort Pulse Laser Ocular Effects" which is part of your collaborative program on laser retinal effects.

Please let me know if you need any further information.

Sincerely yours,

James Fujimoto

James G. Fujimoto
Professor of Electrical Engineering

JGF:cyk

Report for the Air Force Office of Scientific Research
Grant No. F49620-93-1-0301

Mechanisms & Diagnostics of Ultrashort Pulse Laser Ocular Effects
1 October 1993 - 30 September 1994

Principal Investigator: James G. Fujimoto
Massachusetts Institute of Technology

Summary

The objective of our program is to investigate the mechanisms of ultrashort pulse laser retinal injury and to develop and apply new diagnostics for the assessment of retinal injury. During the past contract period, we have focussed on the development of a new diagnostic technique called optical coherence tomography (OCT) for the noninvasive measurement of ocular and retinal structure.

Noninvasive Imaging of Retinal Structure using Optical Coherence Tomography

Working in collaboration with investigators at MIT Lincoln Laboratory and the New England Eye Center, we have developed technology for performing optical coherence tomography on patients and have begun a survey study on human subjects with different retinal diseases. Optical coherence tomography (OCT) is a new non-invasive diagnostic which provides cross-sectional images of tissue with 10 μm longitudinal resolution. The time-of-flight delay of light reflected from different depths in the retina is determined with high sensitivity and high resolution using low-coherence interferometry. Two-dimensional tomographs of optical backscattering in the eye are obtained in a manner analogous to ultrasound B-scan. We have developed a high speed OCT instrument optimized for clinically relevant tomography of the human retina. Imaging is performed in a manner compatible with slit-lamp indirect ophthalmoscopy so that optical tomography may be accomplished simultaneously with normal ophthalmic examination.

We have used OCT *in vivo* to examine over 200 patients with a variety of retinal diseases. In patients with macular pathology, the cross-sectional view provided by OCT is particularly useful in evaluating full and partial-thickness macular holes, detachments of the neurosensory retina and retinal pigment epithelium, macular edema, and macular degeneration. Quantitative measurements of retinal thickness and the extent of retinal detachments with OCT enable objective monitoring of diabetic retinopathy and conditions involving retinal detachment. OCT can also profile the thickness of the retinal nerve fiber

layer with high resolution, which is potentially important for the assessment of glaucoma progression. Preliminary studies of measurement reproducibility have been performed in a cross-section of patients with various stages of glaucoma, and OCT results have been correlated with visual field testing and fundus photography. These studies suggest that OCT has the potential to become a standard clinical diagnostic in ophthalmology.

In-Vivo Imaging of the Evolution of Retinal Laser Lesions using Optical Coherence Tomography

Working in collaboration with investigators from the Armstrong Laboratory at Brooks Air Force Base, the Medical Center of Lubeck Germany, and Duke University, we have performed the first studies which use OCT to noninvasively measure the evolution of retinal lesions produced by different laser retinal exposure parameters.

The knowledge of the morphology and healing response of ocular laser effects is almost entirely based on histopathological findings. Preparational artifacts and only rough pin-point sampling of the time course of these effects limit our current understanding of the biophysical-, medical- and safety aspects of laser-generated effects in the eye. Optical coherence tomography (OCT) provides an approach for studying the initial evolution and the biological response of laser retinal effects. Laser injury from pulses ranging from several 100 ms to 90 fs in duration were investigated. Therapeutically desirable effects such as mild and heavy retinal argon-laser coagulations, side effects [illegible]- and preretinal hemorrhages and highly localized ultrashort laser pulse effects in th[illegible] were produced in rhesus monkey eyes and imaged at times between a few seconds and several days after exposure using on line OCT. Video ophthalmoscopy during the actual experimental procedure, fundus photography, as well as light microscopy of the laser effects at related times post exposure, were performed and correlated with the OCT images.

Preliminary results show the potential and limitations of OCT as a non-invasive *in vivo* diagnostic tool. Structural changes such as gross tissue destruction or pre- and subretinal hemorrhages are clearly visible and easily localizable with a lateral and axial resolution on the order of 10 μm. Thermal effects in the neural retina including sub- and intraretinal edema, even if bearly visible ophthalmoscopically, are identifiable in the OCT images and can be monitored on a second time scale. Ultrashort laser pulse effects are only visible with OCT if the localized damage in the retinal pigment epithelium and the outer retina leads to changes in the tissue structure such as leakage, edema or microdisruption.

Report for the Air Force Office of Scientific Research
Grant No. F49620-93-1-0301

Mechanisms & Diagnostics of Ultrashort Pulse Laser Ocular Effects
1 October 1993 - 30 September 1994

Principal Investigator: James G. Fujimoto
Massachusetts Institute of Technology

Publications

1. J. A. Izatt, M. R. Hee, G. M. Owen, and J. G. Fujimoto, "Optical coherence microscopy in scattering media," *Opt. Lett.* **19**, 590-592, April 1994.
2. J. A. Izatt, M. R. Hee, E. A. Swanson, C. P. Lin, D. Huang, J. S. Schuman, C. A. Puliafito, and J. G. Fujimoto, "Micron-resolution imaging of the anterior eye with optical coherence tomography," *Archives of Ophthalmology*, in press.
3. M. R. Hee, J. A. Izatt, E. A. Swanson, D. Huang, J. S. Schuman, C. P. Lin, C. A. Puliafito, and J. G. Fujimoto, "Optical coherence tomography for micron-resolution ophthalmic imaging," *IEEE Engineering in Medicine & Biology*, in press.
4. M. R. Hee, J. A. Izatt, E. A. Swanson, D. Huang, C. P. Lin, J. S. Schuman, C. A. Puliafito, and J. G. Fujimoto, "Optical coherence tomography of the human retina," *Archives of Ophthalmology*, in press.

Abstracts and Conference Presentations

1. J. G. Fujimoto, J. A. Izatt, M. R. Hee, D. Huang, E. A. Swanson, C. P. Lin, and C. A. Puliafito, "Biological imaging using optical coherence and transillumination tomography," invited paper presented at the 1993 Annual Meeting of the Optical Society of America/ILS-IX, Toronto, Canada, October 3-8, 1993.
2. J. A. Izatt, M. R. Hee, G. Owen, G. Tearney, E. A. Swanson, and J. G. Fujimoto, "Optical coherence microscopy," Advances in Optical Imaging and Photon Migration Topical Meeting, Orlando, FL, March 21-23, 1994, paper WC1.
3. M. R. Hee, J. A. Izatt, D. Huang, E. A. Swanson, C. P. Lin, J. S. Schuman, C. A. Puliafito, and J. G. Fujimoto, "Micron-resolution optical coherence tomography of the human eye," Advances in Optical Imaging and Photon Migration Topical Meeting, Orlando, FL, March 21-23, 1994, paper WA4.
4. J. A. Izatt, M. R. Hee, D. Huang, E. A. Swanson, C. P. Lin, J. S. Schuman, C. A. Puliafito, and J. G. Fujimoto, "High-speed *in vivo* retinal imaging with optical coherence tomography," Technical Digest of the Annual Meeting of the Association for Research in Vision and Ophthalmology, ARVO'94, Sarasota, FL, May 1-6, 1994, paper 2208, p. 1729.
5. M. R. Hee, J. A. Izatt, E. A. Swanson, D. Huang, C. P. Lin, J. S. Schuman, C. A. Puliafito, J. Inderfurth, R. Birngruber, and J. G. Fujimoto, "*In vivo* optical coherence tomography of the anterior segment," Technical Digest of the Annual Meeting of the Association for Research in Vision and Ophthalmology, ARVO'94, Sarasota, FL, May 1-6, 1994, paper 3811, p. 2078.

6. J. A. Izatt, M. R. Hee, G. M. Owen, G. Tearney, E. A. Swanson, and J. G. Fujimoto, "Optical coherence microscopy," Technical Digest of the Conference on Lasers and Electro-Optics, CLEO'94, Anaheim, CA, May 8-13, 1994, paper CTuA4.

7. J. G. Fujimoto, J. A. Izatt, M. R. Hee, B. Bouma, E. A. Swanson, C. P. Lin, and C. A. Puliafito, "Biological imaging using optical coherence tomography," presented at the Fifth International Conference on Laser Applications in Life Sciences (LALS'94), Minsk, Republic of Belarus, June 28-July 2, 1994, plenary presentation.

8. B. Bouma and J. G. Fujimoto, "Nonlinear propagation effects in ultrashort pulse generation," presented at International Workshop on Singularities in Patterns and Collapse: Applications to Semiconductor Lasers and Critical Self-focusing of Ultra-Short Optical Pulses, University College Cork, Cork, Ireland, August 21-26, 1994.

9. J. G. Fujimoto, J. A. Izatt, M. R. Hee, B. Bouma, E. A. Swanson, C. P. Lin, and C. A. Puliafito, "Biological imaging using optical coherence tomography and microscopy," European Quantum Electronics Conference (EQEC'94), Amsterdam, August 28-September 2, 1994.

10. M. R. Hee, J. A. Izatt, S. A. Boppart, J. G. Fujimoto, E. A. Swanson, C. P. Lin, J. S. Schuman, C. Wong, and C. A. Puliafito, "Examination of the retina with optical coherence tomography," submitted for oral presentation at the Biomedical Optics Symposium, Photonics West'95, San Jose, CA, February 4-10, 1995.

11. G. J. Tearney, M. R. Hee, J. A. Izatt, B. Bouma, J. G. Fujimoto, M. B. Brezinski, J. F. Southern, R. R. Anderson, and E. A. Swanson, "Optical coherence tomography in multiply scattering tissue," submitted for oral presentation at the Biomedical Optics Symposium, Photonics West'95, San Jose, CA, February 4-10, 1995.

12. R. Birngruber, M. R. Hee, S. A. Boppart, J. G. Fujimoto, E. A. Swanson, C. A. Toth, C. D. DiCarlo, C. P. Cain, G. D. Noojin, and W. P. Roach, "*In vivo* imaging of the development of linear and non-linear retinal laser effects using optical coherence tomography in correlation with histopathological findings," submitted for oral presentation at the Biomedical Optics Symposium, Photonics West'95, San Jose, CA, February 4-10, 1995.

13. C. D. DiCarlo, S. A. Boppart, M. R. Hee, J. G. Fujimoto, D. A. Gagliano, E. A. Swanson, A. B. Cox, R. Amnotte, A. B. Smith, and W. P. Roach, "A new noninvasive imaging technique for cataract evaluation in the rhesus monkey," submitted for oral presentation at the Biomedical Optics Symposium, Photonics West'95, San Jose, CA, February 4-10, 1995.

Principal Investigator Annual Data Collection (PIADC) Survey Form

Please submit the requested data for the period **1 October 1993 through 30 September 1994**. Request you follow the data requirements and format instructions below. This data is due to your AFOSR program manager NLT 30 September 1994.

NOTE: If there is insufficient space on this survey to meet your data submissions, please submit additional data in the same format as identified below.

PI DATA

Name (Last, First, MI): Fujimoto, James G.

Institution: Mass. Institute of Technology

Contract/Grant No.: F49620-93-1-0301

AFOSR USE ONLY
Project/Subarea
_____/____

NX _____

FY _____

NUMBER OF CONTRACT/GRANT CO-INVESTIGATORS

Faculty 1 Post Doctorates 1 Graduate Students 1 Other _____

PUBLICATIONS RELATED TO AFOREMENTIONED CONTRACT/GRANT

NOTE: List names in the following format: Last Name, First Name, MI

Include: Articles in peer reviewed publications, journals, book chapters, and editorships of books.

Do Not Include: Unreviewed proceedings and reports, abstracts, "Scientific American" type articles, or articles that are not primary reports of new data, and articles submitted or accepted for publication, but with a publication date outside the stated time frame.

Name of Journal, Book, etc.: see attached

Title of Article: _____

Author(s): _____

Publisher (if applicable): _____

Volume: _____ Page(s): _____ Month Published: _____ Year Published: _____

Name of Journal, Book, etc.: _____

Title of Article: _____

Author(s): _____

Publisher (if applicable): _____

Volume: _____ Page(s): _____ Month Published: _____ Year Published: _____

HONORS/AWARDS RECEIVED DURING CONTRACT/GRANT LIFETIME

Include: All honors and awards received during the lifetime of the contract or grant, and any life achievement honors such as (Nobel prize, honorary doctorates, and society fellowships) prior to this contract or grant.

Do Not Include. Honors and awards unrelated to the scientific field covered by the contract/grant.

Honor/Award: National Academy of Sciences Baker Award for Initiatives in Research Year Received: 1990

Honor/Award Recipient(s): James G. Fujimoto

Awarding Organization: National Academy of Sciences

Honor/Award: Optical Society of America Fellow Year Received: 1993

Honor/Award Recipient: James G. Fujimoto

Awarding Organization: Optical Society of America

Honor/Award: Promotion to Professor Year Received: 1994

Honor/Award Recipient: James G. Fujimoto

Awarding Organization: Massachusetts Institute of Technology

AFOSR Technology Transfer/Transition Information for 1994

Directorate: Chemistry and Life Sciences
Program Manager: William P. Roach

Grant # or Lab Task #: F49620-93-1-0301

PI or Lab Task Manager : James G. Fujimoto

PI telephone #: (617) 253-8528

Institution or AF Lab: Massachusetts Institute of Technology
Department of Electrical Engineering
and Computer Science

Address: Research Laboratory of Electronics
Office 36-361
Cambridge, MA 02139

What is transitioned/transferred? (Biefly describe your basic research idea, result, theory, methodology, process, device, fact, knowledge, software etc., which significantly influences the direction of a customer's applied program in government, industry or academia):

No technology transfer activities
as part of this program

Transitioned to whom (who is the customer?):
Name of applied program:

Organization (company, government agency, institution, etc):

Contact (person's name):

Telephone:

Date of transition (year, month or day):

Goal of applied program:

Purpose of transition (how is the direction of the relevant applied program changed by the transition):

8 Sept 94

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
MONTHLY ACCOUNT STATEMENT
FOR AUGUST 31 1994

ACCOUNT 78353 1

SPONSOR: AIR FORCE AEROSPACE RES.-OSR

PURPOSE: MECHANISMS & DIAGNOSTICS ULTRASHORT PULS
AGREEMENT: F49620-93-1-0301

SUPERVISOR: JAMES G FUJIMOTO

BEGINNING DATE: 04/15/93 AGREEMENT TYPE: 1
TERMINATION DATE: 04/14/94

DEPARTMENT: 267000
RESEARCH LABORATORY OF ELECTRONICS

AUTHORIZED AMT: 84,644.00

	CURRENT MONTH	FISCAL YTD	CUMULATIVE	BUDGET
DIRECT EXPENDITURES				
SALARIES AND WAGES				
FACULTY SALARIES-TENURE-ON			2,721.19	3,631.00
OTHER ACADEMIC STAFF-ON			16,048.61	13,888.00
TECHNICAL OR ADMIN SUPPORT-ON		3.50	2,178.84	1,777.00
GRADUATE STUDENT STAFF-ON				7,810.00
RESEARCH ASSISTANT-ON			4,554.67	
TOTAL SALARIES AND WAGES		3.50	25,503.31	27,106.00
EMPLOYEE BENEFITS				
BILLING ON OFF UROP				
E.B. RATES 43.10% 46.30% 6.50%		1.51	11,091.68	11,673.00
OPERATING EXPENSES				
TRAVEL			1,907.96	1,500.00
MATERIALS & SERVICES			2,705.09	4,875.00
ALLOCATED EXPENSE		1.45	954.38	1,364.00
BOOKS			298.75	
EQUIPMENT RENTAL-NO O/H			160.00	
MAINT & REPAIRS			194.00	
OFFICE SUPPLIES			15.75	
PUBLICATIONS		50.00	304.50	
XEROX EXPENSE			847.00	
ELECTRICAL COMPONENTS			93.86	
PETTY CASH			4.00	
POSTAGE MAILING & SHIPPING			99.46	
TEL-BASIC MONTHLY SERVICE			392.01	
TEL-LOCAL CALLS			150.96	
TEL-TOLL CALLS			1,250.99	
TOTAL OPERATING EXPENSES		51.45	9,378.71	7,739.00
EQUIPMENT				
EQUIPMENT-NO OVERHEAD			11,565.65	9,449.00
COMPUTATION EXPENSES				
SOFTWARE			60.00	
TOTAL DIRECT EXPENDITURES		56.46	57,599.35	55,967.00
INDIRECT EXPENDITURES				
INDIRECT EXPENSE				
INDIRECT EXPENSES ON OFF				
BILLING RATES (B/R) 52.00% 12.05%		29.36	25,377.98	28,677.00
TOTAL EXPENDITURES		85.82	82,977.33	84,644.00
UNEXPENDED BALANCE			1,666.67	
ACCOUNTING USE ONLY				
BILLINGS TO SPONSOR				
BILLED TO DATE			84,644.00-	
UNBILLED COST			1,666.67-	